

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
19 April 2001 (19.04.2001)

PCT

(10) International Publication Number
WO 01/26610 A1

(51) International Patent Classification⁷: A61K 6/00, 7/00, A01N 25/34

(21) International Application Number: PCT/US00/27775

(22) International Filing Date: 6 October 2000 (06.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/158,674 8 October 1999 (08.10.1999) US

(71) Applicant (for all designated States except US): THE UNIVERSITY OF AKRON [US/US]; 302 E. Buchtel Avenue, Akron, OH 44325 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SMITH, Daniel [US/US]; 2988 Ridgeline Trail, Stow, OH 44224 (US). RENEKER, Darrell [US/US]; 300 Hampshire Road, Akron, OH 44313 (US). KATAPHINAN, Woraphon [US/US]; 805 Yale Street, #8, Akron, OH 44311 (US). DABNEY, Sally [US/US]; 227 N. Firestone Boulevard, Akron, OH 44301 (US).

(74) Agents: SKOGLUND, Rodney et al.; Renner, Kenner, Greive, Bobak, Taylor & Weber, First National Tower, 16th Floor, Akron, OH 44308 (US).

(81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- *With international search report.*
- *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/26610 A1

(54) Title: ELECTROSPUN SKIN MASKS AND USES THEREOF

(57) Abstract: A skin mask for affecting a skin condition comprises a fibrous membrane comprising one or more fibers that have been electrostatically spun and applied directly onto the three-dimensional topography of the skin to form the membrane. The skin covering or mask containing one or more polymers and, optionally, one or more preferably medically useful additives for protecting and/or healing the skin. The skin mask is generated on the skin by directly electrospinning one or more polymeric fibers onto the skin surface.

ELECTROSPUN SKIN MASKS AND USES THEREOF

TECHNICAL FIELD

This invention relates to a skin care product and, more particularly, to a
5 cosmetic skin care mask for the treatment of any of a number of skin conditions wherein
additives added to the skin are likely to aid in such treatment or wherein the absorption of
excess moisture or oils from the skin is likely to aid in such treatment. Specifically, the
present invention relates to a skin care mask produced by electrospinning polymeric
material, with or without various additives having skin healing, skin cleansing, or other
10 therapeutical or medical properties, into one or more fibers to be applied or deposited
directly to the skin, preferably without the use of any intermediate fabrication steps. Once
the function of the additives or the fibers have been performed, the mask may be peeled
or otherwise removed from the skin.

15

BACKGROUND OF THE INVENTION

The technique of electrospinning, also known within the fiber forming industry
as electrostatic spinning, of liquids and/or solutions capable of forming fibers, is well
known and has been described in a number of patents as well as in the general literature.

The process of electrospinning generally involves the creation of an electrical
20 field at the surface of a liquid. The resulting electrical forces create a jet of liquid which
carries electrical charge. These electrically charged jets of liquid may be attracted to a
body or other object at a suitable electrical potential. As the liquid jet is forced farther and
farther toward the object, it elongates. As it travels away from the liquid reservoir, it
steadily dries and hardens, thereby forming a fiber. The drying and hardening of the liquid
25 jet into a fiber may be caused by cooling of the liquid, i.e., where the liquid is normally
a solid at room temperature; evaporation of a solvent, e.g., by dehydration, (physically
induced hardening); or by a curing mechanism (chemically induced hardening).
Heretofore, the fibers produced by electrospinning techniques have necessarily been
collected on a suitably located charged receiver and subsequently removed from it as
30 needed.

Fibers produced by this process have been used in a wide variety of
applications, but no such fibers have ever been produced for use as skin care masks.
Generally, electrospun fibers are known, from U.S. Patent Nos. 4,043,331 and 4,878,908,

to be particularly useful in forming non-woven mats suitable for use in wound dressings. One of the major advantages of using electrostatically spun fibers in wound dressings, is that very thin fibers can be produced having diameters, usually on the order of about 100 nanometers to about 25 microns, and more preferably, on the order of about 500 5 nanometers to about 5 microns. Thus, these fibers can be collected and formed into non-woven mats of any desired shape and thickness. It will be appreciated that, because of the very small diameter of the fibers, a mat with very small interstices and a high surface area per unit mass, two characteristics that are important in determining the porosity of the mat, can be produced. Still further, U.S. Patent Nos. 4,043,331 and 4,878,908 suggest that such 10 dressings have the advantage that they are usually sufficiently porous to allow interchange of oxygen and water vapor between the atmosphere and the surface of a wound.

Besides providing variability as to the diameter of the fibers or the shape, thickness, or porosity of any non-woven mat produced therefrom, the ability to electrospin the fibers also allows for variability in the composition of the fibers, their density of 15 deposition and their inherent strength. By selectively choosing the composition of the fibers being electrospun, it will be appreciated that fibers having different physical or chemical properties may be obtained. This can be accomplished either by spinning a liquid containing a plurality of components, each of which may contribute a desired characteristic to the finished product, or by simultaneously spinning, from multiple liquid 20 sources, fibers of different compositions that are then simultaneously deposited to form a mat. The resulting wound dressing mat, of course, would consist of intimately intermingled fibers of different material. A further alternative noted in the U.S. patents is to produce a wound dressing mat having a plurality of layers of different fibers of 25 different materials (or fibers of the same material but different characteristics, e.g. diameter), as by, for example, varying with time the fibers being deposited on the receiver.

Thus, U.S. Patent Nos. 4,043,331 and 4,878,908 make it clear that strong, non-woven mats comprising a plurality of fibers of organic, namely polymeric, material produced by electrostatically spinning the fibers from a liquid consisting of the material or precursor thereof is known in the art for use as wound dressings. However, these fibers 30 must necessarily be collected on a suitably charged receiver and subsequently removed therefrom. While U.S. Patent No. 4,043,331 in particular has attempted to provide an improved wound dressing for use on a surface wound by providing a strong, non-woven mat of electrospun, polymeric fibers, it essentially treats the electrospun fibrous mat

formed like a piece of gauze used in a bandage to protect a surface wound and does not offer any application advantage over traditional non-electrospun fiber bandages other than those advantages provided by the use of such small diameter, electrospun fibers as noted hereinabove. There is also no reference to any other applications for this fibrous mat other than for medical applications such as wound dressings or vascular stents.

5 Current skin care masks are generally applied as topical creams, lotions or ointments to deliver medically useful additives. Some masks may include dusts or liquid sprays. No such skin masks use nanofibers to deliver these additives however.

10 More importantly, dusts and liquid sprays may be more likely than fibrous materials to migrate into sensitive areas of the body such as the nose and eyes where the skin mask is being applied to the face.

15 While attempts have been made heretofore to provide wound dressing and other medical devices from electrospun fibers, the art has not suggested other desired and needed applications. Nor has the art suggested how to directly apply the electrospun fibers directly to the skin without intermediate fabrication steps such as using a transient, charged receiver to first collect the fibers into a mat prior to applying them to the wound.

Therefore, the need continues to exist for a cosmetic skin mask of electrospun fibers that can be applied gently and painlessly as well as directly to the skin to provide healing or skin care treatment to the skin.

20

SUMMARY OF INVENTION

It is, therefore, an object of the present invention to provide an improved skin care mask for the treatment of the skin.

25 It is another object of the present invention to provide an improved skin care mask, as above, comprising one or more fibers that are electrostatically spun to form the mask.

It is still another object of the present invention to provide an improved skin care mask, as above, wherein the fibers are applied directly to the skin in a more gentle and painless manner.

30 It is yet another object of the present invention to provide an improved skin mask, as above, which can incorporate various medically useful, skin care additives into the fibers forming the mask.

It is still another object of the present invention to provide an improved skin care mask, as above, which can be readily applied in any size, shape or thickness desired.

It is a further object of the present invention to provide an improved method for treating certain skin conditions of a patient.

5 It is still a further object of the present invention to provide a method for treating a skin condition, as above, wherein fibers forming a skin mask are directly applied to the skin.

It is yet a further object of the present invention to provide a method for treating a skin condition, as above, wherein the skin mask produced is readily peelable or 10 removable.

It is still another object of the present invention to provide a method for treating a skin condition, as above, wherein the skin mask is capable of removing moisture or oils from the skin and/or capable of adding medically useful agents to the skin.

15 At least one or more of the foregoing objects, together with the advantages thereof over the known art relating to electrostatic fiber spinning and skin care products, which shall become apparent from the specification that follows, are accomplished by the invention as hereinafter described and claimed.

20 In general, the present invention provides a skin mask for affecting a skin condition comprising a fibrous membrane comprising one or more fibers that have been electrostatically spun and applied directly onto the three-dimensional topography of the skin to form the membrane. That is, the electrospun fibers of the present invention are preferably not first collected on a suitably charged receiver and subsequently stripped therefrom, but rather are applied directly to the topography of the skin, providing for a more gentle and painless manner of application. Furthermore, the fibers have been found 25 to be capable of including both soluble and insoluble additives therein. Thus, medically useful skin care additives may be incorporated in the liquid forming the fibers, either as a solution or a dispersion. The electrospun fibers can be applied directly to the surface of the skin to form a protective layer on areas of the skin to be treated or protected.

30 Other aspects of the invention are achieved in a method for treating a skin condition comprising the steps of electrostatically spinning one or more fibers and directly assembling the electrospun fibers onto the skin in the form of a skin covering or mask without the use of a transient, charged receiver or other intermediate fabrication step. For those fibers containing medically useful additives, the additives may leach, diffuse, or be

otherwise transferred to the skin and, after the additives have performed their function(s), the covering or mask may be removed as by peeling or other removal methods from the skin.

5

EMBODIMENT FOR CARRYING OUT THE INVENTION

As noted hereinabove, the present invention is directed toward a cosmetic skin covering or mask containing one or more polymers and, optionally, one or more medically useful additives for protecting and/or healing the skin. The skin mask is generated on the skin by directly electrospinning one or more polymeric fibers onto the skin surface. These very thin fibers (i.e., nanofibers) containing the additives provide a larger surface area per unit mass for delivering the additives to the skin than would conventional creams, lotions or ointments, and can deliver the additives in a painless manner. The mask may remain on the skin for a period of time as desired to allow the additives to function, or the additives may be moisture activated with the application of a moist, warm cloth. After the additives have performed their function, the mask may be peeled or otherwise removed from the skin. Importantly, the addition of the additives to the liquid to be electrospun into the fiber (i.e., the spin dope) does not prevent the formation of a covering for the skin using electrospinning techniques.

The polymeric covering or skin mask formed is generally formulated from one or more fibers comprising any of a variety of fluid absorbant, or biodegradable, or water resistant polymers that can be optionally blended with any of a number of medically important skin treating additives. Essentially any polymeric materials soluble in aqueous or organic solvents and suitable for electrospinning into fibers can be employed in the present invention. The preferred choice of polymer(s) to be employed will greatly depend upon the treatment of the skin desired. Thus, the choice of polymers will contribute to the choice of treatment protocol from many possibilities. As an example, polycaprolactone is a biodegradable polymer and will partially absorb moisture from the skin. Alternatively, poly(hydroxy ethyl methacrylate) will absorb more moisture and still slowly convert to a hydrogel in the presence of moisture. Still further, polyethylenimine (PEI) will form salts with α -hydroxy acids currently used in many skin care products. Therefore, spun salts of PEI will function as a delivery system for these acids to the skin. Of course, other additives as set forth hereinbelow may instead of or with the α -hydroxy acids. Essentially

any organic or aqueous soluble polymer or any dispersions of such polymer with a soluble or insoluble additive suitable for topical treatment of the skin may be employed.

As suggested hereinabove, other additives, either soluble or insoluble, may also be included in the liquid(s) to be electrospun into the fibers. Preferably, these additives are medically important topical additives provided in at least effective amounts for the treatment of the skin. Such amounts depend greatly on the type of additive and the physical properties of the polymer(s) employed, and skin condition to be treated. Generally, however, such additives can be incorporated in the fibers in amounts ranging from trace amounts (less than 0.1 parts by weight per 100 parts polymer) to 500 parts by weight per 100 parts polymer, or more. Examples of such additives include, but are not limited to, aspirin; α -hydroxy acids including lactic acid and glycolic acid; retinoids, including all trans-retinol, etc.; DNA proteins, synthetic polypeptides, vitamin E; fragrances for use in aroma therapy and the like; and oil absorbing polymers such as those commercially available under the tradename Polytrap. Other additives such as oils, soaps, or medication for the treatment of any of a number of skin conditions such as acne or various rashes, can be applied broadly or in patterns to provide additional treatment to selected areas of the skin. Antioxidants and antimicrobial additives as well as analgesics such as lidocaine, soluble or insoluble antibiotics such as neomycin, thrombogenic compounds, nitric oxide releasing compounds such as sydnonimines and NO-complexes that promote skin healing may also be employed in the present invention. Still other additives include carvone and insoluble additives such as waterlok and cellulose. Insect repellants and other physical barriers to insects or bugs may also be incorporated.

Prior studies have shown that PEI, when used in non-fiber form, may stabilize all trans retinol and protect the skin from photooxidation. It is believed that the same characteristics can be found using electrospun fibers. Both retinol and antioxidant activity is welcome in the treatment of the skin. Essentially any polymer or additive suitable for the treatment of any of a number of skin conditions wherein additives added to the skin are likely to aid in such treatment or wherein the absorption of excess moisture or oils from the skin is likely to aid in such treatment, can be employed.

It will be appreciated that the fibers can produce a number of different types of coverings or masks depending upon how the fibers are produced. For instance, the liquid to be electrospun into the plurality of fibers may be a mixture of one or more organic or aqueous soluble polymers and one or more skin care or treatment additives.

Thus, one fluid could provide the entire mask. However, it is also envisioned that fibers of different compositions could be spun together or in sequential layers to provide a suitable mask of one or more layers.

As discussed earlier, one of the major advantages of using electrospun fibers,
5 is that these fibers can be produced having very small diameters, usually on the order of about 100 nanometers to about 5 micron, and more preferably, on the order of about 100 nanometers to about 1 micron. Thus, given that these "nanofibers" can be formed into non-woven masks of any desired shape and thickness relatively rapidly, their usefulness and desirability as skin care masks can readily be appreciated.

10 Because of the very small diameter of the fibers, a mask with very small interstices and high surface area per unit mass is produced. It will be appreciated that the higher surface area allows for far greater utilization and quickens the rate of transfer of the additive(s) to the skin which thereby benefits from the full potential of the additive. The electrospun polymeric masks of the present invention have high surface areas of preferably
15 at least $5 \text{ m}^2/\text{g}$, and more preferably, approximately $100 \text{ m}^2/\text{g}$ for efficient fluid absorption and dermal delivery.

20 The electrospun fiber-formed masks of the present invention are lightweight, may be oxygen and moisture permeable, and resistant against airborne contaminants such as dust, microbes, or other infectious agents which might be carried by the air currents or otherwise affect the care of the skin. The ability of the fibers to transport and deliver medically useful additives to the skin can be controlled through the choice of polymer as a carrier, density and thickness of the applied mask, and/or layering of different fiber compositions.

25 With respect to the fibers, it will be understood that the fibers should preferably be dry so as to have sufficient strength in forming the mask. However, in some instances, a wet fiber may be employed. Such wet fibers are generally softer and conform to the surface of the skin better. In any event, the ability to electrospin very thin fibers (i.e., nanofibers) directly onto the skin surface and to place medically useful additives into the solutions used to create the fibers, thereby incorporating the additives into the polymeric
30 fibers, are very important advances leading to the present invention. The polymer(s) or additive(s) employed in fiber(s) may directly absorb excess moisture or oils from the skin. Moreover, the direct application of the fibers means that the fibers can be advantageously placed in intimate contact with the skin, enabling efficient removal of dead cells, fluid or

bacteria from the skin. Direct contact with the surface of the skin will also enable improved additive delivery to the skin. Finally, it will be appreciated that direct application provides for improved and, in fact, inherent sterility of the fibers.

It will be appreciated that essentially any organic or aqueous solvent suitable
5 for dissolving the desired polymer and capable of being electrospun can be employed. Non-limiting examples of such suitable solvents include acetone, tetrahydrofuran, ethanol or other low molecular weight alcohols, and water. It will further be appreciated that the skin treating additives may be soluble or insoluble in the solvent employed. Where the additives are insoluble, they may be encapsulated within the fibers using the
10 electrospinning techniques described. It has been found that fibers produced from these electrospinning techniques with such additives still impart the desired properties of the additive and yet maintain the porous membrane-like properties of the nanofibrous skin mask as described.

It will further be appreciated that essentially any device known in the art
15 capable of electrospinning fibers may be used to electrospin the fibers and deliver the fibers to the skin in forming the skin mask. Preferably, the device will be portable and handheld. One such device is described in a provisional application filed on the same day of this application. The disclosure of that device and other aspects of the application are incorporated herein by reference.

Thus it should be evident that the skin mask and methods for treatment of
20 certain skin conditions as set forth in the present invention are highly effective in protecting and treating the skin and certain conditions thereof. The invention is particularly suited for use as cosmetic facial masks, but is not necessarily limited thereto. For example, other applications may include the use of the membranes or masks for skin
25 beautification for such things as general cosmetics, coverage of burns, scars, scratches, bruises, moles, tattoos, fill indentations or dimples, or the like. The product may further be used to cover cellulite, acne, scars, cuts, cysts, and the like, or to hide varicose veins, dry skin spots, surgical stitches, and the like. The mask and method of the present invention can further be used separately with other equipment, methods and the like, as
30 well as for the manufacture of other skin masks and related materials. For example, electrospun fibers of appropriate composition may be used to provide protection of the skin against other threats such as "last ditch" protection against toxic substances such as chemical warfare agents.

In addition, it is envisioned that the skin masks of the present invention may be used to color or tone the skin such as by coloring or tinting the fibers for general skin cosmetic use. The coloring of the fibers could also be used to provide novelty or specialty coloring to the skin such as "glow in the dark" or flourescent coloring.

5 The size and shape of the mask or membrane can be readily controlled, and it is further envisioned that the shape of the mask may be controlled or predetermined via the use of templates and the like as is known in the art with other skin creams.

Based upon the foregoing disclosure, it should now be apparent that the use of the skin mask as described herein will carry out the objects set forth hereinabove. It is, 10 therefore, to be understood that any variations evident fall within the scope of the claimed invention and thus, the selection of specific component elements can be determined without departing from the spirit of the invention herein disclosed and described. In particular, the skin masks produced according to the present invention are not necessarily limited to those described in any particular embodiment. Thus, the scope of the invention 15 shall include all modifications and variations that may fall within the scope of the attached claims.

CLAIMS

What is claimed is:

1. 1. A mask for affecting a skin condition, the mask comprising:
 2. a fibrous membrane comprising one or more electrospun fibers, wherein the one or more fibers are applied directly onto the three-dimensional topography of the skin to form the membrane.
1. 2. The mask according to claim 1, wherein the fibers are colored.
1. 3. The mask according to claim 1, wherein the membrane has a predetermined shape.
1. 4. The mask according to claim 1, wherein the fibers include a polymer soluble in an aqueous solvent.
1. 5. The mask according to claim 4, wherein the polymer is biodegradable and will at least partially absorb moisture from the skin.
1. 6. The mask according to claim 4, wherein the polymer is poly(ethylenimine).
1. 7. The mask according to claim 1, wherein the electrospun fibers include an additive for conditioning or protecting the skin.
1. 8. The mask according to claim 7, wherein the additive is medical useful for treating the skin.
1. 9. The mask according to claim 7, wherein the additive is selected from the group consisting of aspirin, α -hydroxy acids, retinoids, DNA proteins, synthetic polypeptides, vitamin E, fragrances, oil absorbing polymers, oils, soaps, antioxidants, antimicrobial additives, insect repellents, and cosmetic additives.
1. 10. The mask according to claim 7, wherein the additive is incorporated into the one or more fibers in amounts ranging from trace amounts to 500 parts by weight per 100 parts polymer.

- 1 11. The mask according to claim 1, further comprising a second fibrous membrane
- 2 forming a layer over the original fibrous membrane.
- 1 12. The mask according to claim 1, wherein the fibers have diameters ranging from
- 2 about 100 nanometers to about 5 microns.
- 1 13. The mask according to claim 1, wherein the mask have a surface area of at least 5
- 2 m^2/g .
- 1 14. The mask according to claim 1, wherein the additives may be absorbed into the skin.
- 1 15. A method for treating a skin condition comprising:
 - 2 electrostatically spinning one or more fibers; and
 - 3 directly assembling the electrostatically spun fibers onto the skin without the
 - 4 use of a transient, charged receiver.
- 1 16. The method according to claim 15, wherein the step of assembling includes forming
- 2 a mask or membrane of fibers on the skin.
- 1 17. The method according to claim 15, wherein the step of spinning includes the step of
- 2 forming a fiber from a liquid of one or more organic or aqueous soluble polymers
- 3 and one or more additives for the treatment of the skin.
- 1 18. The method according to claim 17, wherein the additives are selected from the group
- 2 consisting of aspirin, α -hydroxy acids, retinoids, DNA proteins, synthetic
- 3 polypeptides, vitamin E, fragrances, oil absorbing polymers, oils, soaps,
- 4 antioxidants, antimicrobial additives, insect repellents, and cosmetic additives.
- 1 19. A method for providing a color to the skin comprising the method of claim 15.

1 20. A method for covering burns, scars, scratches, bruises, cuts, moles, tattoos, acne,
2 cellulite, cysts, varicose veins, dry skin spots, stitches, and skin conditions
3 comprising the method of claim 15.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/27775

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 6/00, 7/00; A01N 25/34

US CL :424/410, 402

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/410, 402

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST ALL DATA BASES

search terms: mask, polymer, polyethylenimine, active agent, fibrous membrane

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,844,017 A (JAMIOKOWSKI et al.) 01 December 1998, entire document	1-20
A	US 4,074,366 A (CAPOZZA) 21 February 1978, entire document	1-20
A	US 4,043,331 A (MARTIN et al.) 23 August 1977, entire document.	1-20

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search

07 DECEMBER 2000

Date of mailing of the international search report

15 FEB 2001

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

ISIS GHALI

Telephone No. (703) 308-1235

